

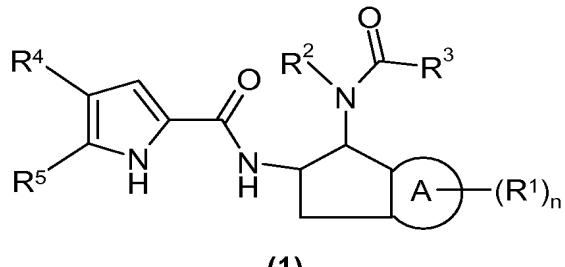
Application No. 10/567,801
Amendment Dated 03/13/2007
Reply to Office Action of 02/13/2007

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A compound of formula (1):



wherein:

R⁴ and R⁵ together are either -S-C(R⁶)=C(R⁷)- or -C(R⁷)=C(R⁶)-S- ;

R⁶ and R⁷ are independently selected from hydrogen, halo, nitro, cyano, hydroxy, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, carboxy, carbamoyl, (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkoxy and (1-4C)alkanoyl;

A is phenylene or heteroarylene;

n is 0, 1 or 2;

R¹ is independently selected from halo, nitro, cyano, hydroxy, carboxy, carbamoyl, N-(1-4C)alkylcarbamoyl, N,N-((1-4C)alkyl)₂carbamoyl, sulphamoyl, N-(1-4C)alkylsulphamoyl, N,N-((1-4C)alkyl)₂sulphamoyl, -S(O)_b(1-4C)alkyl (wherein b is 0,1,or 2), -OS(O)₂(1-4C)alkyl, (1-4C)alkyl, (2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkoxy, (1-4C)alkanoyl, (1-4C)alkanoyloxy, hydroxy(1-4C)alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy and -NHSO₂(1-4C)alkyl;

or, when n is 2, the two R¹ groups, together with the carbon atoms of A to which they are attached, may form a 4 to 7 membered saturated ring, ~~optionally containing 1 or 2 heteroatoms independently selected from O, S and N, and optionally being substituted by one or two methyl groups;~~

one of R² and R³ is selected from R_{Na}, and the other is selected from R_{Nb};

R_{Na}: (1-3C)alkyl, halo(1-3C)alkyl, dihalo(1-3)alkyl, trifluoromethyl, hydroxy(1-3C)alkyl, dihydroxy(2-3C)alkyl, cyano(1-3C)alkyl (optionally substituted on alkyl with hydroxy), methoxymethyl, ethoxymethyl, methoxyethyl, methoxymethoxymethyl, dimethoxyethyl, (hydroxy)(methoxy)ethyl, 5- and 6-membered acetals and mono- and di-methyl derivatives

Application No. 10/567,801
Amendment Dated 03/13/2007
Reply to Office Action of 02/13/2007

thereof, (amino)(hydroxy)(2-3C)alkyl, (aminocarbonyl)(hydroxy)(2-3C)alkyl, (methylaminocarbonyl)(hydroxy)(2-3C)alkyl, (dimethylaminocarbonyl)(hydroxy)(2-3C)alkyl, (methylcarbonylamino)(hydroxy)(2-3C)alkyl, (methylS(O)_p-)(hydroxy)(2-3C)alkyl (wherein p is 0, 1 or 2);

R_{Nb}: (1-4C)alkyl, halo(1-4C)alkyl, dihalo(1-4C)alkyl, trifluoromethyl, hydroxy(1-4C)alkyl, dihydroxy(2-4C)alkyl, trihydroxy(3-4C)alkyl, cyano(1-4C)alkyl (optionally substituted on alkyl with hydroxy), (1-4C)alkoxy(1-4C)alkyl, (1-4C)alkoxy(1-4C)alkoxy(1-4C)alkyl, di[(1-4C)alkoxy](2-4C)alkyl, (hydroxy)[(1-4C)alkoxy](2-4C)alkyl, 5- and 6-membered acetals and mono- and di-methyl derivatives thereof, (amino)(hydroxy)(2-4C)alkyl, (aminocarbonyl)(hydroxy)(2-4C)alkyl, ((1-4C)alkylaminocarbonyl)(hydroxy)(2-4C)alkyl, (di(1-4C)alkylaminocarbonyl)(hydroxy)(2-4C)alkyl, ((1-4C)alkylcarbonylamino)(hydroxy)(2-4C)alkyl, ((1-4C)alkylS(O)_p-(hydroxy)(2-4C)alkyl (wherein p is 0, 1 or 2);

wherein any alkyl or alkoxy group within any group in R_{Na} and R_{NB} may also optionally be substituted on an available carbon atom with a hydroxy group (provided that said carbon atom is not already substituted by a group linked by a heteroatom);

provided that if R² is (1-3C)alkyl or (1-4C)alkyl then R³ is not (1-4C)alkyl or (1-3C)alkyl; or a pharmaceutically acceptable salt or pro-drug thereof.

2. (original) A compound of formula (1) as claimed in Claim 1, or a pharmaceutically acceptable salt or pro-drug thereof, wherein R² is selected from R_{Na}, and R³ is selected from R_{Nb}, wherein R_{Na} and R_{Nb} are as defined in Claim 1.

3. (cancelled)

4. (previously presented) A compound of formula (1) as claimed in Claim 1, or a pharmaceutically acceptable salt or pro-drug thereof, wherein n is 0.

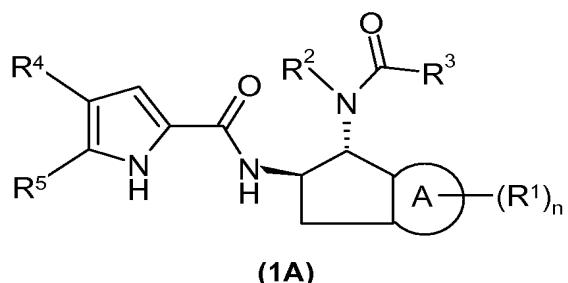
5. (previously presented) A compound of formula (1) as claimed in Claim 1, or a pharmaceutically acceptable salt or pro-drug thereof, wherein R⁶ and R⁷ are independently selected from hydrogen and halo.

Application No. 10/567,801
Amendment Dated 03/13/2007
Reply to Office Action of 02/13/2007

6. (previously presented) A compound of formula (1) as claimed in Claim 1, or a pharmaceutically acceptable salt or pro-drug thereof, wherein R⁶ and R⁷ are independently selected from hydrogen and chloro.

7. (previously presented) A compound of formula (1) as claimed in Claim 1, or a pharmaceutically acceptable salt or pro-drug thereof, wherein R_{NA} is selected from (1-4C)alkyl, hydroxy(1-4C)alkyl, and (1-4C)alkoxy(1-4C)alkyl.

8. (currently amended) A compound of formula (1) as claimed in Claim 1, or a pharmaceutically acceptable salt or pro-drug thereof, which is a compound of formula (1A):



wherein R¹ to R⁷, A and n are as defined in claim 1.

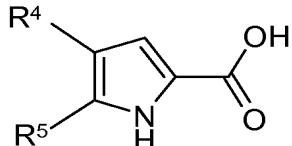
9. (previously presented) A pro-drug of a compound of formula (1) as claimed in Claim 1, which pro-drug is an in-vivo hydrolysable ester.

10. (original) A pharmaceutical composition which comprises a compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in claim 1 in association with a pharmaceutically-acceptable diluent or carrier.

11-15. (cancelled)

16. (withdrawn) A process for the preparation of a compound of formula (1) as claimed in claim 1, which process comprises:

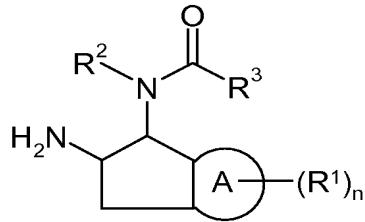
reacting an acid of the formula (2):



Application No. 10/567,801
Amendment Dated 03/13/2007
Reply to Office Action of 02/13/2007

(2)

or an activated derivative thereof; with an amine of formula (3):



and thereafter if necessary:

- i) converting a compound of the formula (1) into another compound of the formula (1);
- ii) removing any protecting groups;
- iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.

17. (previously presented) A compound of formula (1), or a pharmaceutically acceptable salt or pro-drug thereof, selected from:

2-chloro-N-{(1*R*,2*R*)-1-[(methoxyacetyl)(methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2-chloro-N-{(1*R*,2*R*)-1-[[3-hydroxy-2-(hydroxymethyl)propanoyl](methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
ethyl 3-[((1*R*,2*R*)-2-{{(2-chloro-6*H*-thieno[2,3-*b*]pyrrol-5-yl)carbonyl}amino}-2,3-dihydro-1*H*-inden-1-yl)(methyl)amino]-3-oxopropanoate;
2-[((1*R*,2*R*)-2-{{(2-chloro-6*H*-thieno[2,3-*b*]pyrrol-5-yl)carbonyl}amino}-2,3-dihydro-1*H*-inden-1-yl)(methyl)amino]-2-oxoethyl acetate;
2-chloro-N-{(1*R*,2*R*)-1-[glycoloyl(methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2-chloro-N-{(1*R*,2*R*)-1-[glyceroyl(methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2-chloro-N-{(1*R*,2*R*)-1-[(2*S*)-2,3-dihydroxypropanoyl](methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2-chloro-N-{(1*R*,2*R*)-1-[(2*R*)-2,3-dihydroxypropanoyl](methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2-chloro-N-{(1*R*,2*R*)-1-[(3-hydroxypropanoyl)(methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;

Application No. 10/567,801
Amendment Dated 03/13/2007
Reply to Office Action of 02/13/2007

2-chloro-N-((1*R*,2*R*)-1-[glycoloyl(2-hydroxyethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2-chloro-N-((1*R*,2*R*)-1-[(2*R*)-2-hydroxypropanoyl](methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2-chloro-N-((1*R*,2*R*)-1-[(2*S*)-2-hydroxypropanoyl](methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2,3-dichloro-N-((1*R*,2*R*)-1-[(2*R*)-2,3-dihydroxypropanoyl](methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide
2,3-dichloro-N-((1*R*,2*R*)-1-[(2*S*)-2,3-dihydroxypropanoyl](methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide;
(2*S*)-N¹-((1*R*,2*R*)-2-{[(2-chloro-6*H*-thieno[2,3-*b*]pyrrol-5-yl)carbonyl]amino}-2,3-dihydro-1*H*-inden-1-yl)-2-hydroxy-N¹-methylsuccinamide;
(2*S*)-N¹-((1*R*,2*R*)-2-{[(2,3-dichloro-4*H*-thieno[3,2-*b*]pyrrol-5-yl)carbonyl]amino}-2,3-dihydro-1*H*-inden-1-yl)-2-hydroxy-N¹-methylsuccinamide;
2,3-dichloro-N-((1*R*,2*R*)-1-[(2*S*)-2-hydroxybutanoyl](methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide;
2,3-dichloro-N-((1*R*,2*R*)-1-[(2*S*)-2-hydroxy-3-methylbutanoyl](methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide;
2,3-dichloro-N-((1*R*,2*R*)-1-[(2*S*)-4-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-2-hydroxybutanoyl](methyl)amino)-2,3-dihydro-1*H*-inden-2-yl}-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide;
2,3-dichloro-N-((1*R*,2*R*)-1-[(2*R*)-2-hydroxy-3-(methylthio)propanoyl](methyl)amino)-2,3-dihydro-1*H*-inden-2-yl}-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide;
tert-butyl {(2*S*)-3-[((1*R*,2*R*)-2-{[(2,3-dichloro-4*H*-thieno[3,2-*b*]pyrrol-5-yl)carbonyl]amino}-2,3-dihydro-1*H*-inden-1-yl)(methyl)amino]-2-hydroxy-3-oxopropyl}carbamate;
2,3-dichloro-N-((1*R*,2*R*)-1-[(2*S*)-3-cyano-2-hydroxypropanoyl](methyl)amino)-2,3-dihydro-1*H*-inden-2-yl}-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide;
N-((1*R*,2*R*)-1-[(*N*-acetylseryl)(methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-2-chloro-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
N-((1*R*,2*R*)-1-[(*N*-acetylseryl)(methyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-2,3-dichloro-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide;
2,3-dichloro-N-((1*R*,2*R*)-1-[methyl(L-seryl)amino]-2,3-dihydro-1*H*-inden-2-yl}-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide hydrochloride;
2-chloro-N-((1*R*,2*R*)-1-[methyl(L-seryl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide hydrochloride;

Application No. 10/567,801
Amendment Dated 03/13/2007
Reply to Office Action of 02/13/2007

(2S)-*N*¹-((1*R*,2*R*)-2-{[(2-chloro-6*H*-thieno[2,3-*b*]pyrrol-5-yl)carbonyl]amino}-2,3-dihydro-1*H*-inden-1-yl)-2-hydroxy-*N*¹-methylpentanediamide;
(2S)-*N*¹-((1*R*,2*R*)-2-{[(2,3-dichloro-4*H*-thieno[3,2-*b*]pyrrol-5-yl)carbonyl]amino}-2,3-dihydro-1*H*-inden-1-yl)-2-hydroxy-*N*¹-methylpentanediamide;
2-chloro-*N*-{(1*R*,2*R*)-1-[(2*S*)-2-hydroxy-3-methoxypropanoyl](methyl) amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2,3-dichloro-*N*-{(1*R*,2*R*)-1-[(2*S*)-2-hydroxy-3-methoxypropanoyl](methyl) amino]-2,3-dihydro-1*H*-inden-2-yl}-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide;
2,3-dichloro-*N*-{(1*R*,2*R*)-1-[(2*R*)-2-hydroxy-3-(methylsulfonyl)propanoyl](methyl) amino]-2,3-dihydro-1*H*-inden-2-yl}-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide;
N-{(1*R*,2*R*)-1-[(2*S*)-3-amino-2-hydroxypropanoyl](methyl) amino]-2,3-dihydro-1*H*-inden-2-yl}-2,3-dichloro-4*H*-thieno[3,2-*b*]pyrrole-5-carboxamide hydrochloride;
(2*S*)-*N*¹-((1*R*,2*R*)-2-{[(2,3-dichloro-4*H*-thieno[3,2-*b*]pyrrol-5-yl)carbonyl]amino}-2,3-dihydro-1*H*-inden-1-yl)-2-hydroxy-*N*¹,*N*⁴-dimethylsuccinamide;
(2*S*)-*N*¹-((1*R*,2*R*)-2-{[(2,3-dichloro-4*H*-thieno[3,2-*b*]pyrrol-5-yl)carbonyl] amino}-2,3-dihydro-1*H*-inden-1-yl)-2-hydroxy-*N*¹,*N*⁴,*N*⁴-trimethylsuccinamide;
2-chloro-*N*-{(1*R*,2*R*)-1-[glyceroyl(2-hydroxyethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2-chloro-*N*-{(1*R*,2*R*)-1-[(2*R*)-2,3-dihydroxypropanoyl](2-hydroxyethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide;
2-chloro-*N*-{(1*R*,2*R*)-1-[(2*S*)-2,3-dihydroxypropanoyl](2-hydroxyethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-6*H*-thieno[2,3-*b*]pyrrole-5-carboxamide.

18. (withdrawn) A method of producing a glycogen phosphorylase inhibitory effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (1) as claimed in claim 1.

19. (withdrawn) A method of treating type 2 diabetes, insulin resistance, syndrome X, hyperinsulinaemia, hyperglucagonaemia, cardiac ischaemia or obesity in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (1) as claimed in claim 1.

Application No. 10/567,801
Amendment Dated 03/13/2007
Reply to Office Action of 02/13/2007

20. (withdrawn) A method of treating type 2 diabetes in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (1) as claimed in claim 1.